

Title:

Predicting the Response of Breast Cancer to Neoadjuvant Chemotherapy Using a Mechanically Coupled Reaction-Diffusion Model

Authors:

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Abstract:

While there is mature data on mathematical models to describe tumor growth and response to therapy, they are often not of the form that can be easily applied to clinical data to generate testable predictions in individual patients. Thus, there is a clear need to develop and apply clinically-relevant oncological models that are amenable to available patient data and yet retain the most salient features of response prediction. In this effort, we utilize a biomechanically-coupled mathematical model of tumor growth that is initialized and constrained by MRI data, obtained early in the course of therapy, to predict the response from individual patients with breast cancer to neoadjuvant chemotherapy (NAC). MRI was performed on 28 breast cancer patients exhibiting a varying degree of responsiveness to NAC. Anatomical, DCE- and DW-MRI data were acquired prior to beginning NAC and after one cycle of NAC. DCE-MRI data sets at each time point were used to define a tumor ROI and diffusion data for the tumor voxels was transformed to estimate tumor cell number. Using a patient-specific spatiotemporal tumor growth modeling framework, tumor response is parameterized using data from before and after the first cycle of therapy, and the model is driven forward in time to predict tumor burden at the conclusion of therapy. Model reconstructed parameters and predictions are retrospectively assessed for prognostic value in predicting patients that eventually respond (i.e., achieve pathological complete response) or do not respond to NAC. Using our mechanics-coupled modeling approach, we are able to discriminate, after the first cycle of therapy, breast cancer patients that would eventually achieve a complete pathological response and those who would not, with an area under the receiver operating characteristic curve of 0.81. This work provides considerable promise for predictive modeling centered on integrating quantitative in vivo MRI data with biomechanical models of tumor growth as a prognostic indicator of response to therapy.

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